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TECH CENTER 1600/2900

Application No. 08/858,087

Attorney's Docket No. 000475-205

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REMARKS

Entry of the foregoing, re-examination and reconsideration of the application identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.112 and in light of the remarks which follow are respectfully requested. Claims 16-17, 19-31 and 35-39 are pending in this application. Claim 16 has been amended. New claims 40 and 41 have been added. Claims 17, 19-21, 27-31 and 35-39 are withdrawn from further consideration, as being drawn to non-elected inventions and species. The examined claims are 16 and 22-26, all of which currently stand rejected.

Amendments

Claim 16 has been amended to include the limitation "...wherein the intersection of inlet flow paths with the main flow paths is at an upstream angle of less than 90°..."

Support for the amendment to claim 16 and addition of new claims 40 and 41 can be found, at least at page 9, lines 21-27. No prohibited new matter has been added by the amendment or the new claims.

The Examiner courteously pointed out that in Claim 16, the word "a" in line 3 after "comprising" should be deleted. As requested, this typographical error has been corrected by the present amendment, and no prohibited new matter has been introduced by this amendment. Accordingly, Applicants request that the objection to Claim 16 be withdrawn.

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Withdrawal of Previous Rejections

Applicants also note with appreciation that the previous rejections, as set forth in the prior Office Action dated July 24, 2000, under 35 U.S.C. §§ 112, 102 and 103 have all been withdrawn in light of the claim amendment presented in Paper No. 21.

I. Double Patenting Rejection

Claims 16 and 22-26 have been provisionally rejected under the judicially created doctrine of double patenting over claims 16 and 22-26 of copending application number 09/080,546. Since this is a provisional rejection, Applicants will submit a terminal disclaimer at the appropriate time if necessary.

II. Rejection of Claim 16 under 35 U.S.C. § 102(a)

Claims 16 stands rejected under 35 U.S.C. § 102(a) as being anticipated by Li *et al.* (*Analytical Chemistry*, 69:1564-1568, April 15, 1997). Applicants respectfully traverse this rejection. Claim 16 has been amended as discussed above.

Li *et al.* relates to transport, manipulation, and reaction of biological cells on-chip using electrokinetic effects. However, Li *et al.* does not teach that the "intersection of inlet flow paths with the main flow path is at an upstream angle of less than 90°." As pointed out in the Applicants' specification at page 9 line 21 to page 10, line 2, when the inlet flow path and the main flow path intersect at an upstream angle of 90° or greater, the turbulence generated at the intersection of the inlet flow path with the main flow path may result in damage or rupture to the cells. Such damage or rupture is to be avoided if an accurate

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determination of the effect of the candidate compound is to be determined. In addition, lysis of the cell may cause the main flow path to become clogged, preventing subsequent observations of additional cells.

According to the relevant standards, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Thus, since the Li *et al.* reference does not disclose the limitation as discussed above, it does not anticipate the currently claimed invention.

Applicants further reserve the right to file a suitable Declaration under 37 C.F.R. § 1.131, as appropriate. In addition, while not at issue here, Applicants reserve the right, as appropriate, to establish that the Li *et al.* reference was published on behalf of the inventors.

For the above reasons, Applicants respectfully submit that withdrawal of the rejection under 35 U.S.C. §102(a) would be appropriate.

III. Rejection of Claim 22 under 35 U.S.C. § 103(a)

Claim 22 stands rejected under 35 U.S.C. § 103(a), as being unpatentable over Li *et al.* in view of Tracey *et al.* (*IEEE Transactions of Biomedical Engineering*, 42(8):751-761 (1995)). Applicants respectfully traverse this rejection.


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Initially, a proper analysis of the obviousness/nonobviousness of the claimed invention by the USPTO requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should practice the claimed process; and (2) whether the prior art would also have revealed that in so practicing, there would be a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. *In re Sernaker*, 217 U.S.P.Q. 1, at 5 (Fed. Cir. 1983); and *In re Vaeck*, 20 USPQ2d 1438, 1442 (CAFC 1991).

When so analyzed, it is clear that this rejection is in error because the cited references provide no reasonable basis for the skilled artisan to either combine the references or to predict success.

Li et al. is discussed above. *Tracey et al.*, even in combination with *Li et al.* still fails to teach or suggest the methods of the invention where the "intersection of inlet flow paths with the main flow path is at an upstream angle of less than 90°."

The Examiner acknowledges that *Li et al.* also differs from the claimed invention because they did not show that the cells were lymphocytes. The Examiner relies on *Tracey et al.* for disclosure of devices which may be used in blood cell studies. *Tracey et al.* relates to a silicon micromachined device for use in blood cell deformability studies. However, while *Tracey et al.* merely speculates that their initial objective of erythrocyte measurement may be extended to leucocyte analysis, motivation to combine the teachings of *Li et al.* with *Tracey et al.* to produce the methods of the claimed invention is still lacking.



In fact, Tracey *et al.* does not even show the successful extension of their methods to lymphocytes, but merely speculates that it might be "possible" with "larger channel cross-sections and more complex imaging" at page 759, lines 12-15 of column 2. In fact, Tracey *et al.* teaches away from the use of lymphocytes in their system at page 759, lines 15-28 of column 2, when they discuss why it is not possible to image platelets using their system, and that further experimentation was required to develop such methods. Thus, Tracey *et al.* does not teach or suggest how lymphocytes might be studied, even using their own system, much less the system of Li *et al.* When viewed under the appropriate standard for obviousness, Applicants submit that absent both the motivation to combine references and a reasonable expectation of success, the claimed invention is simply not *prima facie* obvious over the Li *et al.* See *In re Vaeck*, supra.

Moreover, even if one assumes *arguendo* that the cited Li *et al.* and Tracey *et al.* references were combined, because the cited Li *et al.* reference is directed to a different type of microfluidic device, Applicants maintain that the skilled artisan could not have predicted *a priori* that blood cell deformability studies could be successfully employed in a microfluidic device of Li *et al.* based solely on the cited references because it was not predictable what the effect would be of carrying out experiments in lymphocytes in microfluidic device of Li *et al.*

For all of the reasons discussed above, Applicants submit that this rejection is in error. Accordingly, withdrawal of this rejection would be appropriate.




IV. Rejection of Claims 23-26 under 35 U.S.C. § 103(a)

Claims 23-26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Li *et al.*, in view of Tracey *et al.*, as applied to Claim 22 previously, and further in view of Wilding *et al.* (Clinical Chemistry, 40(1):43-47 (1994)). Applicants respectfully traverse this rejection.

Li *et al.* and Tracey *et al.* are discussed above. Li *et al.* and Tracey *et al.*, even when combined with Wilding *et al.*, still fail to teach or suggest the methods of the invention.

As indicated by the Examiner, both of these references fail to disclose that the flow paths are coated. However, Wilding *et al.* does not remedy this shortcoming. Wilding *et al.* does not relate to channels with branching or fluidic networks. At page 47, column 1, they merely extrapolate from a straight channel experiment as to the possibility of multi-channel devices. Wilding *et al.* do not teach or suggest that a microfluidic device, such as claimed in the present invention, should be coated. None of the secondary references, when used alone or in combination, provide the motivation to arrive at the methods of the present invention. Even if, *ad arguendo*, these references were combined, there is still no reasonable expectation of success in achieving the methods of the present invention.

For the reasons set forth above, Li *et al.*, either alone or in combination with Tracey *et al.* and/or Wilding *et al.* does not teach or suggest the methods of the claimed invention. Therefore, this rejection is in error. Accordingly, Applicants request that this rejection be withdrawn.

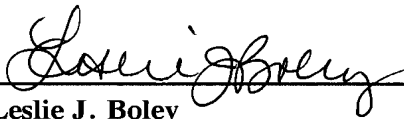


From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

If there are any questions concerning this paper or the application in general, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

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Attachment to Amendment dated September 19, 2001

Marked-up Claim 16

16. (four times amended) A method of observing the effect of one or more candidate compounds on cells in a microfluidic device comprising:

(a) providing a microfluidic device comprising a main flow path comprising [a] an outlet, at least two inlet flow paths and a detection zone, wherein at least one inlet flow path intersects and merges with the main flow path at the detection zone, wherein the intersection of inlet flow paths with the main flow path is at an upstream angle of less than 90°;

(b) applying into the microfluidic device at least one cell which flows into a first inlet flow path and a candidate compound to a second inlet flow path;

(c) inducing flow of the cells and the candidate compound toward the outlet;

(d) allowing the at least one cell to mix with the candidate compound in the detection zone; and

([f] e) observing the effect of the candidate compound on the cells in the detection zone.

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